

8. REGULATIONS AND ADVISORIES

The international, national, and state regulations and guidelines regarding 1,4-dioxane in air, water, and other media are summarized in Table 8-1.

ATSDR has derived an acute-duration inhalation MRL of 2 ppm for 1,4-dioxane based on a LOAEL of 50 ppm for eye irritation in humans (Young et al. 1977). No NOAEL was defined in the study. An uncertainty factor of 30 was used (3 for using a minimal LOAEL and 10 to protect sensitive populations).

ATSDR has derived a chronic-duration inhalation MRL of 1 ppm for 1,4-dioxane based on a NOAEL of 111 ppm for liver effects in rats (Torkelson et al. 1974). No LOAEL was defined in the study. The MRL was derived using the PBPK model developed by Reitz et al. (1990). An uncertainty factor 30 was used (3 for using dosimetric adjustments and 10 to protect sensitive populations). The chronic-duration inhalation MRL of 1 ppm also has been adopted as the intermediate-duration inhalation MRL.

ATSDR has derived an acute-duration oral MRL of 4 mg/kg/day for 1,4-dioxane based on a NOAEL of 370 mg/kg/day for nasal effects in male rats (JBRC 1998a). The LOAEL was 1,010 mg/kg/day in males and 1,040 mg/kg/day in females. An uncertainty factor of 100 was used (10 for the protection of sensitive populations and 10 for animal to human extrapolation).

ATSDR has derived an intermediate-duration oral MRL of 0.6 mg/kg/day for 1,4-dioxane based on a NOAEL of 60 mg 1,4-dioxane/kg/day for liver effects in male rats (JBRC 1998b). The LOAEL was 150 mg/kg/day in males and 200 mg/kg/day in females. An uncertainty factor of 100 was used (10 for the protection of sensitive populations and 10 for animal to human extrapolation).

ATSDR has derived a chronic-duration oral MRL of 0.1 mg/kg/day for 1,4-dioxane based on a NOAEL of 9.6 mg 1,4-dioxane/kg/day for liver effects in male rats (Kociba et al. 1974). The LOAEL was 94 mg/kg/day in males and 148 mg/kg/day in females. An uncertainty factor of 100 was used (10 for the protection of sensitive populations and 10 for animal to human extrapolation).

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Table 8-1. Regulations and Guidelines Applicable to 1,4-Dioxane

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification	Group 2B ^a	IARC 1999
WHO	No data		
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA)	20 ppm ^b	ACGIH 2003
NIOSH	REL (30-minute ceiling TWA)	1 ppm ^c	NIOSH 2004
	IDLH	500 ppm	
EPA	Hazardous air pollutant		EPA 2004d 42USC7412
OSHA	PEL (8-hour TWA) for general industry	100 ppm ^b	OSHA 2004c 29CFR1910.1000, Table Z-1
	PEL (8-hour TWA) for construction industry	100 ppm ^b	OSHA 2004b 29CFR1926.55, Appendix A
	PEL (8-hour TWA) for shipyard industry	100 ppm ^b	OSHA 2004a 29CFR1915.1000, Table Z
b. Water			
EPA	Drinking water standards and health advisories		EPA 2004b
	1-Day HA for a 10-kg child	4.0 mg/L	
	10-Day HA for a 10-kg child	0.4 mg/L	
	10 ⁻⁴ cancer risk	0.3 mg/L	
c. Food			
FDA	Indirect food additive for use only as a component of adhesives		FDA 2003 21CFR175.105
d. Other			
ACGIH	Carcinogenicity classification	Group A3 ^d	ACGIH 2003
EPA	Carcinogenicity classification	B2 ^e	IRIS 2004
	RfC	No data	
	RfD	No data	
	Oral slope factor	1.1x10 ⁻² (mg/kg/day) ⁻¹	EPA 2004e 40CFR372.65
	Drinking water unit risk	3.1x10 ⁻⁷ (µg/L) ⁻¹	
	Community right-to-know; release reporting; effective date	01/01/1987	
	Designated as a hazardous substance pursuant to Section 112 of the Clean Air Act and Section 3001 of RCRA		
	Reportable quantity	100 pounds	EPA 2004a 40CFR302.4

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Agency	Description	Information	Reference
<u>NATIONAL</u> (cont.)			
	Hazardous waste identification	U108	EPA 2004c 40CFR261, Appendix VIII
NTP	Carcinogenicity classification	Reasonably anticipated to be a human carcinogen	NTP 2002
<u>STATE</u>			
a. Air			
	No data		
b. Water			
	Drinking water guidelines		HSDB 2004
Florida		5 µg/L	
Maine		70 µg/L	
Massachusetts		50 µg/L	
Michigan		3 µg/L	
North Carolina		7 µg/L	
c. Food			
	No data		
d. Other			
	No data		

^aGroup 2B: Possibly carcinogenic to humans.

^bSkin designation: Potential significant contribution to the overall exposure by the cutaneous route, including mucous membranes and the eyes, either by contact with vapors, or of probable greater significance, by direct skin contact with the substance.

^cPotential occupational carcinogen.

^dGroup A3: Confirmed animal carcinogen with unknown relevance to humans.

^eB2: probable human carcinogen.

ACGIH = American Conference of Governmental Industrial Hygienists; CFR = Code of Federal Regulations; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; HA = Health Advisory; HSDB = Hazardous Substances Data Bank; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; RCRA = Resource Conservation and Recovery Act; RfC = reference concentration; RfD = reference dose; TLV = threshold limit values; TWA = time-weighted average; USC = United States Codes; WHO = World Health Organization

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The EPA (IRIS 2004) has not derived a reference dose (RfD) or a reference concentration (RfC) for 1,4-dioxane, but derived an oral slope factor of $1.1 \times 10^{-2} \text{ (mg/kg/day)}^{-1}$ based on the increased incidence of nasal tumors in male Osborne-Mendel rats (NCI 1978). As part of its systematic prioritization process, the EPA is currently re-evaluating the health assessment for 1,4-dioxane (EPA 2004f).